Set	Items	Description
S1	271	AU="KHUDYAKOV Y" OR AU="KHUDYAKOV Y E" OR AU="KHUDYAKOV Y.-E." OR AU="KHUDYAKOV YE" OR AU="KHUDYAKOV YU E" OR AU="KHUDYAKOV YURI" OR AU="KHUDYAKOV YURY" OR AU="KHUDYAKOV YURY E" OR AU="KHUDYAKOV YURI E"
S2	138	AU="KHUDYAKOV Y.E." OR AU="KHUDYAKOV YE" OR AU="KHUDYAKOV YU. E." OR AU="KHUDYAKOV YUE"
S3	57	AU="KHUDYAKOV YURI E" OR AU="KHUDYAKOV YURY" OR AU="KHUDYAKOV YURY E"
S4	289	S1 OR S2 OR S3
S5	90309	HEPATITIS(W)C(W)VIRUS
S6	1085	MOSAIC(W)(PROTEIN? ? OR PEPTIDE? ?)
S7	97	S4 AND S5
S8	339257	GENOTYPE? ?
S9	2260895	IMMUNOASSAY OR ASSAY OR ELISA OR EIA OR RIA OR RADIOIMMUNOASSAY OR CHEMILUMINESC?
S10	50	RD S7 (unique items)
S11	14000	S5 AND S8
S12	3968	S11 AND S9
S13	11	S12 AND S6
S14	0	S13 NOT PY>1997
S15	0	RD (unique items)
S16	2257	S12 NOT PY>1997
S17	1086	RD (unique items)
S18	44592	S5/TI
S19	613	S18 AND S17
S20	66704	S8/TI
S21	160	S19 AND S20

?

10/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09023291 96419926 PMID: 8822625
Characterization of the antibody reactivity to synthetic peptides from different parts of the hepatitis C virus **genome.**
Pujol FH; **Khudyakov YE** ; Devesa M; Leon G; Blitz-Dorfman L; Monsalve F; Lambert SB; Kalinina TY; Liprandi F; Fields HA
Laboratorio de Biologia de Virus, CMBC, IVIC, Caracas, Venezuela.
Viral immunology (UNITED STATES) 1996, 9 (2) p89-96, ISSN 0882-8245 Journal Code: AD0
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Infection by **hepatitis C virus** (HCV)*, the aetiologic agent responsible for the majority of non-A-non-B posttransfusion hepatitis, is detected by assaying for antibodies against structural and nonstructural recombinant proteins or synthetic peptides. The aim of this study was to characterize the antibody reactivity of selected sera against antigenic peptides spanning immunodominant regions of the core, NS4 and NS5 HCV proteins. Reactivity to synthetic peptides was determined by enzyme immunoassay (EIA) for 11 selected sera from blood donors (good responders), for 27 selected sera from hemodialysis patients (poor responders), all positive for HCV antibodies (tested by different second and third-generation assays), and for 7 negative sera. Some peptides from the core and the NS4 region were widely recognized by the tested sera. Sera not reactive with core, NS4, or NS5 region by some immunoblot assays exhibited reactivity against peptides from these proteins. Autoimmune reactivity associated with HCV infection was evaluated by using a synthetic peptide derived from the GOR peptide; 8/11 HCV-positive sera were found reactive against this peptide. No correlation was found between reactivity to any of the peptides tested and the presence of HCV RNA in the serum or with HCV genotype. The EIA reactivity of peptides from the core region suggested a multideterminant antigenic structure, where reactivity of each epitope may be differentially affected by neighboring amino acids depending on individual sera. This situation was particularly evidenced in selected sera from poor responder specimens where a more restricted antibody response to core peptides was observed. Reactivity of sera from HCV-infected patients with synthetic peptides from the core, NS4, and NS5 regions indicated the presence of multiple linear epitopes (particularly in the core region) that may be used in a mixture for immunodiagnosis; however, the length and exact position of the synthetic peptides must be chosen carefully.

10/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08733913 95133207 PMID: 7530398
Linear B-cell epitopes of the NS3-NS4-NS5 proteins of the hepatitis C virus **as modeled with synthetic peptides.**
Khudyakov Yu E ; Khudyakova NS; Jue DL; Lambert SB; Fang S; Fields HA
Hepatitis Branch, Centers for Disease Control and Prevention, Atlanta, Georgia 30333.
Virology (UNITED STATES) Jan 10 1995, 206 (1) p666-72, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A set of 150 synthetic peptides spanning the proteins NS3-NS4-NS5 of the **hepatitis C virus** (HCV) was synthesized and tested with a panel of 20 sera obtained from HCV-infected patients. Of 62 peptides prepared from the NS3 region, none exhibited strong antigenic reactivity. Rather, five peptides from this region demonstrated specific reactivity with only 5-10%

of anti-HVC-positive sera. Nonetheless, it is well known that the NS3 region contains strong antigenic epitopes. These epitopes appear to be modeled in a functionally active manner with recombinant proteins and cannot be mimicked properly with short synthetic peptides. This finding suggests that the major NS3 antigenic epitopes are conformationally dependent. Seven of 20 peptides prepared from the NS4 region were immunoreactive. Five peptides from this region demonstrated very strong HCV-specific antigenic reactivity. Four of the five peptides belong to the recognized immunoreactive 5-1-1 region located inside the C100-3 antigen. One peptide demonstrating immunoreactivity with approximately 90% of anti-HCV-positive sera was found outside the C100-3 region at the C-terminal part of the NS4 protein. Of 68 peptides synthesized from the NS5 protein, 30 were immunoreactive. Six of the 30 demonstrated immunoreactivity with 35-50% of anti-HCV-positive sera. Thus, the NS4 and NS5 regions of the HCV polyprotein contain a large number of specific, broadly reactive, linear antigenic epitopes. The highly antigenic reactivity of the NS5 region suggests that this protein may have significant diagnostic potential.

10/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07140523 93324342 PMID: 7687345
Synthetic gene for the hepatitis C virus **nucleocapsid protein.**
Khudyakov YE ; Fields HA; Favorov MO; Khudyakova NS; Bonafonte MT; Holloway B
Hepatitis Branch, Centers for Disease Control, Atlanta, GA 30333.
Nucleic acids research (ENGLAND) Jun 11 1993, 21 (11) p2747-54, ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A synthetic gene encoding the **hepatitis C virus** (HCV) nucleocapsid protein was constructed and expressed in E. coli. To synthesize this gene, we developed a new method that results in the enzymatic synthesis of long polydeoxyribonucleotides from oligodeoxyribonucleotides. The method, designated as the 'Exchangeable Template Reaction' (ETR), uses oligonucleotides as templates for DNA polymerase. A special mechanism was designed to exchange the templates during the polymerase reaction. The mechanism relies on the formation of a single-stranded 3'-protrusion at the 'growing point' of the elongating DNA such that it can be subsequently annealed, in a sequence-specific manner, with the next synthetic oligonucleotide. When annealed to the 3'-protrusion, the added oligonucleotide becomes a template for DNA polymerase, and the protruding 3'-end of the double-stranded DNA is used as the primer. The HCV nucleocapsid gene was assembled with DNA ligase from three fragments synthesized by ETR. The data verify that this method is efficient. The main advantage of ETR is the ability to combine more than two oligonucleotides in one tube together with polymerase and an enzymatic activity that produces a 3'-protrusion (e.g., BstXI) rather than the sequential addition of each component. The data demonstrate that as many as five oligonucleotides can be used simultaneously, resulting in a synthesized DNA fragment of designed sequence. The synthetic gene expressed in E. coli produced a 27 kDa protein that specifically interacted with antibodies from sera obtained from HCV-infected individuals.

10/3,AB/15 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09067905 BIOSIS NO.: 199497076275

Synthesis and antigenic activity of the peptides from the hepatitis C virus **NS4-protein C-terminal region.**
AUTHOR: Semiletov Yu A; Firsova T V; Kuzin S N; **Khudyakov Yu E** ; Shibnev V A
AUTHOR ADDRESS: Res. Inst. Virol., Acad. Med. Sci. Russ., Moscow**Russia
JOURNAL: Bioorganicheskaya Khimiya 19 (11):p1128-1131 1993
ISSN: 0132-3423
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Russian; Non-English
SUMMARY LANGUAGE: Russian; English

ABSTRACT: A set of four peptides from the HCV NS4-protein C-terminal region (aa 1921-1940) were obtained by solid-phase synthesis using activated esters and symmetrical anhydrides of Boc-amino acids. Peptide 1921-1940 has demonstrated a positive reaction in ELISA with individual anti-HCV-positive sera from patients with acute and chronic hepatitis C (80% and 56%, respectively). We analysed the antigenic properties of the peptide 1921-1940 and its fragments and suggested at least two antibody recognizing sites to be contained in this region.

1993

10/3,AB/17 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07669389 Genuine Article#: 194GQ Number of References: 52
Title: Antigenic heterogeneity of the hepatitis C virus **NS4 protein as modeled with synthetic peptides** (ABSTRACT AVAILABLE)
Author(s): Chang JC; Seidel C; Ofenloch B; Jue DL; Fields HA; **Khudyakov YE (REPRINT)**
Corporate Source: CTR DIS CONTROL & PREVENT,HEPATITIS BRANCH, DIV VIRAL & RICKETTSIAL DIS, NATL CTR INFECT DIS/ATLANTA//GA/30333 (REPRINT); CTR DIS CONTROL & PREVENT,HEPATITIS BRANCH, DIV VIRAL & RICKETTSIAL DIS, NATL CTR INFECT DIS/ATLANTA//GA/30333; BOEHRINGER MANNHEIM GMBH,/D-82372 PENZBERG//GERMANY/
Journal: VIROLOGY, 1999, V257, N1 (APR 25), P177-190
ISSN: 0042-6822 Publication date: 19990425
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495
Language: English Document Type: ARTICLE
Abstract: The effect of sequence heterogeneity on the immunologic properties of two strong antigenic regions of the **hepatitis C virus** (HCV) NS4 protein was studied by using a set of 443 overlapping 20-mer synthetic peptides. One antigenic region comprising the cleavage site between NS4a and NS4b (region 5-1-1) was modeled with peptides derived from 73 different known sequences, representing HCV genotypes 1-6. The other antigenic region, designated region 59 and located at the C-terminus of the NS4b protein, was modeled with peptides from 7 known sequences representing genotypes 1-3. All peptides were tested for antigenic reactivity by enzyme immunoassay with a panel of anti-HCV-positive serum specimens representing genotypes 1-5. The data demonstrated that immunoreactive peptides fell into two groups. One group, represented by N-terminal peptides, demonstrated genotype-independent immunoreactivity; the other group, from the central part of region 5-1-1, showed strict genotype specificity. Nineteen peptides from the genotype-independent group strongly immunoreacted with a wide range of serum samples containing antibodies to all 5 HCV genotypes. Twenty-five peptides from the genotype-specific group were found to strongly react with serum containing antibodies only to the genotype from which the peptides were derived. Similar to the N-terminal part of region 5-1-1, peptides derived from region 59

did not show genotype-specific immunoreactivity. Some peptides derived from the central part of region 59 showed very strong and broad antigenic reactivity. Thus, after examining two antigenic regions of the NS4 protein, we identified short sequences that can be used for the efficient detection of either genotype-independent or genotype-specific HCV antibodies.

10/3,AB/25 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0180199 DBA Accession No.: 95-08219 PATENT
Plasmid construction for efficient expression of synthetic genes in Escherichia coli- hepatitis C virus nucleocapsid protein expression
AUTHOR: **Khudyakov Y** ; Fields H A
PATENT ASSIGNEE: Nat.Inst.Health-Bethesda 1995
PATENT NUMBER: WO 9511980 PATENT DATE: 950504 WPI ACCESSION NO.: 95-178872 (9523)
PRIORITY APPLIC. NO.: US 141917 APPLIC. DATE: 931025
NATIONAL APPLIC. NO.: WO 94US12166 APPLIC. DATE: 941025
LANGUAGE: English
ABSTRACT: A vector consisting of, in sequential order: (a) a Shine-Dalgarno nucleotide sequence having a unique restriction endonuclease site; and (b) a synthetically produced protein coding DNA sequence having (i) a translation start codon, (ii) a sequence about equidistant 3' of the translation start codon as the Shine-Dalgarno sequence is 5', which selectively hybridizes with the Shine-Dalgarno sequence to form a hairpin loop in which the start codon is exposed in the loop such that translation is efficiently initiated, and (iii) an adenosine-containing region of a length sufficient to substantially prevent secondary structure of the vector in the region immediately downstream of the hairpin loop, is claimed. Preferably, the DNA sequence encodes **hepatitis C virus** nucleocapsid protein and a restriction endonuclease site not present in the DNA encoding the native protein can be found after the adenosine-containing region. Also claimed are: (1) the vector DNA sequence (sequence specified); (2) a cell which can express a protein encoded by the vector; (3) and a method of producing a protein.

10/3,AB/26 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0174844 DBA Accession No.: 95-01665 PATENT
Solid phase immunoassay using oligonucleotide as label- hepatitis C virus disease, tumor, etc. diagnosis
AUTHOR: Fields H A; **Khudyakov Y E**
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1994
PATENT NUMBER: WO 9426932 PATENT DATE: 941124 WPI ACCESSION NO.: 95-006819 (9501)
PRIORITY APPLIC. NO.: US 61694 APPLIC. DATE: 930513
NATIONAL APPLIC. NO.: WO 94US5407 APPLIC. DATE: 940513
LANGUAGE: English
ABSTRACT: A new method for detecting antigens in a patient's sample comprises: binding the antigens in the sample to a solid surface; contacting the antigens with an immunoreactive ligand (linked to an oligonucleotide (oligo)) to allow reaction of the oligo-linked ligand with the bound antigen; recovering unreacted oligo-linked ligand; and detecting the oligo as proof that the antigen is present. The oligo and the ligand are preferably linked by biotin-streptavidin-biotin and the

oligo is amplified by the polymerase chain reaction or the ligase chain reaction prior to detection. Also new are: (1) detection of an antibody (Ab) in a patient's sample by binding Abs to a solid surface, contacting them with an immunoreactive antigen (linked to an oligo) to allow reaction of the oligo-linked antigen and bound Ab, and detecting the presence of the oligo as proof that Ab is present; (2) a composition of an oligo linked to a protein of disclosed protein sequence; (3) nucleic acid (sequence disclosed); (4) composition of the disclosed protein covalently linked to the nucleic acid; and (5) diagnosis of past or present **hepatitis C virus** infection using (2). (34pp)

10/3,AB/33 (Item 2 from file: 345)
DIALOG(R)File 345:Inpadoc/Fam.& Legal Stat

12874754
Basic Patent (No,Kind,Date): CA 2196195 AA 19960215 <No. of Patents: 006>
METHODS AND COMPOSITIONS FOR DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC HEPATITIS C VIRUS INFECTION (English; French)
Patent Assignee: US HEALTH (US)
Author (Inventor): FIELDS HOWARD A (US); KHUDYAKOV YURY E (US)
IPC: *C07K-007/08; C07K-007/06; C07K-014/18; G01N-033/576
CA Abstract No: *124(23)315043Z;
Derwent WPI Acc No: *C 96-129330;
Language of Document: English
Patent Family:

Patent No	Kind	Date	Applic No	Kind	Date	
AU 9532053	A1	19960304	AU 9532053	A	19950728	
CA 2196195	AA	19960215	CA 2196195	A	19950728	(BASIC)
EP 804473	A1	19971105	EP 95928202	A	19950728	
JP 10506382	T2	19980623	JP 95506653	A	19950728	
US 5670310	A	19970923	US 282758	A	19940729	
WO 9604300	A1	19960215	WO 95US9599	A	19950728	

Priority Data (No,Kind,Date):
US 282758 A 19940729
WO 95US9599 W 19950728

10/3,AB/38 (Item 3 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00410800
METHODS AND COMPOSITIONS FOR DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC HEPATITIS C VIRUS **INFECTION**
PROCEDES ET COMPOSITIONS SERVANT A EFFECTUER UN DIAGNOSTIC DIFFERENTIEL D'INFECTION AIGUE ET CHRONIQUE PAR LE VIRUS DE L'HEPATITE C
Patent Applicant/Assignee:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA represented by THE
Inventor(s):
FIELDS Howard A
KHUDYAKOV Yury E
Patent and Priority Information (Country, Number, Date):
Patent: WO 9604300 A1 19960215
Application: WO 95US9599 19950728 (PCT/WO US9509599)
Priority Application: US 94282758 19940729
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English

Fulltext Word Count: 11000

English Abstract

The present invention provides antigenic peptides which bind anti- HCV antibodies for the differential diagnosis of acute and chronic HCV infection. The invention further provides a method of differentiating acute and chronic **hepatitis C virus** infection in a subject comprising: a) contacting an antibody-containing sample from the subject with one or more of the peptides selected from the group consisting of peptide 59, comprising the amino acids AFASRGNHVSPTHYVPESDA (SEQ ID NO:1), peptide 137, comprising the amino acids MNRLIAFASRGNHVSPTHYV (SEQ ID NO:2) and peptide 138, comprising the amino acids SRGNHVSPTHYVPESDAAAR (SEQ ID NO:3) under conditions that permit binding between the peptide and the antibodies; b) detecting the presence of binding between the peptide and the antibodies; c) contacting the antibody-containing sample from the subject with an amount of peptide 139, comprising the amino acids NHVSPTHYVPESDAAARVTA (SEQ ID NO:4) under conditions that permit binding between the peptide and the antibodies; d) detecting the presence of binding between the peptide and the antibodies; and comparing the strength of the antibody binding of step b) with the strength of the antibody binding of step d), a stronger binding in step b) as compared to the binding in step d) indicating acute **hepatitis C virus** infection and an equivalent binding in both steps b) and d) indicating chronic **hepatitis C virus** infection. The present invention further provides a method of diagnosing a **hepatitis C virus** infection in a subjet comprising contacting an antibody containing sample from the subject with a peptide comprising the amino acids SPTHYV (SEQ ID NO: 5) and determining the presence of binding between the peptide and the antibodies from the sample, the presence of binding between the peptide and the antibodies indicating a **hepatitis C virus** infection.

Japanese Abstract

L'invention concerne des peptides antigeniques se liant a des anticorps anti-HCV, et permettant d'effectuer un diagnostic differentiel d'infection aigue et chronique par HCV. L'invention, de plus, concerne un procede servant a differencier l'infection aigue et l'infection chronique par le virus de l'hepatite C et consistant a: (a) mettre en contact un echantillon contenant l'anticorps, preleve chez le patient, avec un ou plusieurs des peptides selectionnes dans le groupe constitue par le peptide 59, compose des acides amines AFASRGNHVSPTHYVPESDA (SEQ ID NO:1), par le peptide 137, compose des acides amines MNRLIAFASRGNHVSPTHYV (SEQ ID NO:2) et par le peptide 138, compose des acides amines SRGNHVSPTHYVPESDAAAR (SEQ ID NO.3) dans des conditions permettant la liaison entre le peptide et les anticorps; (b) a detecter la presence d'une liaison entre le peptide et les anticorps; (c) a mettre l'echantillon contenant l'anticorps du patient en contact avec une quantite de peptide 139, compose des acides amines NHVSPTHYVPESDAAARVTA (SEQ ID NO:4) dans des conditions permettant la liaison entre le peptide et les anticorps; (d) a detecter la presence d'une liaison entre le peptide et les anticorps et a comparer la force de la liaison de l'anticorps de l'etape (b) avec la force de la liaison de l'anticorps de l'etape (d), une liaison plus forte a l'etape (b) par rapport a la liaison de l'etape (d) indiquant une infection aigue par le virus de l'hepatite C et une liaison equivalente dans les deux etapes (b) et (d) indiquant une infection chronique par le virus de l'hepatite C. L'invention concerne, de plus, un procede de diagnostic d'une infection par le virus de l'hepatite C chez un patient, qui consiste a mettre un echantillon contenant un anticorps, preleve chez le patient, en contact avec un peptide compose des acides amines SPTHYV (SEQ ID NO:5) et a determiner la presence d'une liaison entre le peptide et les anticorps de l'echantillon, la presence d'une liaison entre le peptide et les anticorps indiquant une infection par le virus de l'hepatite C.

10/3,AB/48 (Item 4 from file: 654)
DIALOG(R)File 654:US PAT.FULL.

02693113
Utility
METHODS AND COMPOSITIONS FOR DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC **HEPATITIS C VIRUS** INFECTION
[Antigenic peptides]

PATENT NO.: 5,670,310
ISSUED: September 23, 1997 (19970923)
INVENTOR(s): Fields, Howard A., Marietta, GA (Georgia), US (United States of America)
Khudyakov , Yury E., Atlanta, GA (Georgia), US (United States of America
ASSIGNEE(s): The United States of America as represented by the Department of Health and Human Services, (A U.S. Government Agency), Washington, DC (District of Columbia, US (United States of America)
[Assignee Code(s): 6814]
APPL. NO.: 8-282,758
FILED: July 29, 1994 (19940729)

FULL TEXT: 1479 lines

ABSTRACT

The present invention provides antigenic peptides which bind anti-HCV antibodies for the differential diagnosis of acute and chronic HCV infection. The invention further provides a method of differentiating acute and chronic **hepatitis C virus** infection in a subject comprising: a) contacting an antibody-containing sample from the subject with one or more of the peptides selected from the group consisting of peptide 59, comprising the amino acids AFASRGNHVSPTHYVPESDA (SEQ ID NO:1), peptide 137, comprising the amino acids MNRLIAFASRGNHVSPTHYV (SEQ ID NO:2) and peptide 138, comprising the amino acids SRGNHVSPTHYVPESDAAAR (SEQ ID NO:3) under conditions that permit binding between the peptide and the antibodies; b) detecting the presence of binding between the peptide and the antibodies; c) contacting the antibody-containing sample from the subject with an amount of peptide 139, comprising the amino acids NHVSPTHYVPESDAAARVTA (SEQ ID NO:4) under conditions that permit binding between the peptide and the antibodies; d) detecting the presence of binding between the peptide and the antibodies; and comparing the strength of the antibody binding of step b) with the strength of the antibody binding of step d), a stronger binding in step b) as compared to the binding in step d) indicating acute **hepatitis C virus** infection and an equivalent binding in both steps b) and d) indicating chronic **hepatitis C virus** infection. The present invention further provides a method of diagnosing a **hepatitis C virus** infection in a subject comprising contacting an antibody containing sample from the subject with a peptide comprising the amino acids SPTHYV (SEQ ID NO:5) and determining the presence of binding between the peptide and the antibodies from the sample, the presence of binding between the peptide and the antibodies indicating a **hepatitis C virus** infection.
?

21/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09373647 97339584 PMID: 9196183
Serological determination of hepatitis C virus genotype: **comparison with a standardized genotyping** assay.
Pawlotsky JM; Prescott L; Simmonds P; Pellet C; Laurent-Puig P; Labonne C ; Darthuy F; Remire J; Duval J; Buffet C; Etienne JP; Dhumeaux D; Dussaix E
Department of Bacteriology and Virology, Hopital Henri Mondor, Universite Paris XII, Creteil, France. pawlotsky@univ-paris12.fr
Journal of clinical microbiology (UNITED STATES) Jul 1997, 35 (7) p1734-9, ISSN 0095-1137 Journal Code: HSH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In patients with chronic hepatitis C, determination of **hepatitis C virus** (HCV) **genotype** could be routinely run in the future to tailor treatment schedules. The suitabilities of two versions of a serological, so-called serotyping **assay** (Murex HCV Serotyping **Assay** version 1-3 [SA1-3] and Murex HCV Serotyping **Assay** version 1-6 [SA1-6]; Murex Diagnostics Ltd.), based on the detection of **genotype** -specific antibodies directed to epitopes encoded by the NS4 region of the genome, for the routine determination of HCV **genotypes** were studied. The results were compared with those of a molecular biology-based genotyping method (HCV Line Probe **Assay** [INNO-LiPA HCV]; Innogenetics S.A.), based on hybridization of PCR products onto **genotype** -specific probes designed in the 5' noncoding region of the genome, obtained with pretreatment serum samples from 88 patients with chronic hepatitis C eligible for interferon therapy. Definitive genotyping was performed by sequence analysis of three regions of the viral genome in all samples with discrepant typing results found among at least two of the three assays studied. In all instances, sequence analysis confirmed the result of the INNO-LiPA HCV test. The sensitivity of SA1-3 was 75% relative to the results obtained by the genotyping **assay** . The results were concordant with those of genotyping for 92% of the samples typeable by SA1-3. The sensitivity of SA1-6 was 89% relative to the results obtained by the genotyping **assay** . The results were concordant with those of genotyping for 94% of the samples typeable by SA1-6. Overall, SA1-6 had increased sensitivity relative to SA1-3 but remained less sensitive than the genotyping **assay** on the basis of PCR amplification of HCV RNA. Cross-reactivities between different HCV **genotypes** could be responsible for the mistyping of 8 (SA1-3) and 6% (SA1-6) of the samples. Subtyping of 1a and 1b is still not possible with the existing peptides, but discriminating between subtypes may not be necessary for routine use.

21/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09367201 97330496 PMID: 9186955
A DNA hybridization method for typing hepatitis C virus genotype **2c.**
Biasin MR; Fiordalisi G; Zanella I; Cavicchini A; Marchelle G; Infantolino D
Servizio di Anatomia Patologica, Ospedale Civile, Castelfranco Veneto, Italy.
Journal of virological methods (NETHERLANDS) May 1997, 65 (2) p307-15, ISSN 0166-0934 Journal Code: HQR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A high prevalence of **hepatitis C virus** (HCV) **genotype** 2c (22%)

was detected in sera from 459 italian patients by core-region amplification and hybridization with specific probes by DNA enzyme **immunoassay** . Amplified fragments failed to hybridize with 1a, 1b, 2a, 2b and 3a subtype-specific and 4, 5, 6 type-specific oligonucleotides in 105 patients. Hybridization of these samples with type 2 probe, which recognized all the subtypes sequences, showed evidence for **genotype** 2 distinct from 2a and 2b. Fourteen out of these 105 isolates were cloned and sequenced. The results were consistent with genotyping **assay** . Nucleotide sequences were partially related to types 2a, 2b, 2d, 2e and 2f (87.0-93.5% of identity). The average nucleotide identity was highest for **genotype** 2c (95.87%). On the basis of sequence analysis, subtype 2c specific probe was derived. Hybridization efficiency with the newly designed probe was very high and more than 95% (100/105) of type 2 cases were classified as 2c. Evidence of different outcome of therapy inside the same HCV major type account for the need of accurate subtyping. In this study, amplification of the core region followed by hybridization with highly specific probes enabled distinction between HCV subtypes.

21/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09298556 97281205 PMID: 9135513
Clinical relevance of hepatitis C virus genotypes.
Simmonds P
Department of Medical Microbiology, University of Edinburgh.
Gut (ENGLAND) Mar 1997, 40 (3) p291-3, ISSN 0017-5749
Journal Code: FVT
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

21/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09264049 97123689 PMID: 8968936
Indeterminate results of the second-generation hepatitis C virus **(HCV) recombinant immunoblot** assay **: significance of high-level c22-3 reactivity and influence of HCV** genotypes.
Zein NN; Germer JJ; Wendt NK; Schimek CM; Thorvilson JN; Mitchell PS; Persing DH
Department of Medicine, Mayo Clinic, Rochester, Minnesota 55905, USA.
Journal of clinical microbiology (UNITED STATES) Jan 1997, 35 (1) p311-2, ISSN 0095-1137 Journal Code: HSH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A second-generation recombinant immunoblot **assay** (RIBA 2.0) is used in the United States to confirm infection with **hepatitis C virus** (HCV) in samples that are anti-HCV (enzyme **immunoassay**) positive. In some cases, indeterminate results of RIBA 2.0, which are defined as reactivity to a single antigen species or reactivity limited to two proteins derived from the same coding region of the HCV genome, are encountered. This study was performed to establish the significance of indeterminate RIBA 2.0 results in relation to HCV RNA detection, high positivity for the c22-3 band, and the HCV **genotype** as determined by direct DNA sequencing. Ninety-six samples with indeterminate RIBA 2.0 results were studied. HCV RNA was detected in 21 of 34 (62%) samples with high reactivity to c22-3 and in 8 of 62 (13%) samples with low reactivity to c22-3. The HCV **genotype** distribution in samples that were RIBA 2.0 indeterminate and HCV RNA positive was significantly different from that in samples of a control group with positive results for both the RIBA 2.0 and HCV PCR. These

results suggest that highly positive c22-3 samples are likely to be associated with HCV viremia and that infection with less common HCV **genotypes** is more commonly associated with indeterminate RIBA 2.0 results.

21/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09264022 97123661 PMID: 8968908
New hepatitis C virus **(HCV) genotyping system that allows for identification of HCV** genotypes **1a, 1b, 2a, 2b, 3a, 3b, 4, 5a, and 6a.**
Ohno O; Mizokami M; Wu RR; Saleh MG; Ohba K; Orito E; Mukaide M; Williams R; Lau JY
Department of Public Health, Nagoya City University Medical School, Japan.
Journal of clinical microbiology (UNITED STATES) Jan 1997, 35 (1) p201-7, ISSN 0095-1137 Journal Code: HSH
Contract/Grant No.: AI41219, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Recent studies have focused on whether different **hepatitis C virus** (HCV) **genotypes** are associated with different profiles of pathogenicity, infectivity, and response to antiviral therapy. The establishment of a simple and precise genotyping system for HCV is essential to address these issues. A new genotyping system based on PCR of the core region with **genotype** -specific PCR primers for the determination of HCV **genotypes** 1a, 1b, 2a, 2b, 3a, 3b, 4, 5a, and 6a was developed. A total of 607 samples (379 from Japan, 63 from the United States, 53 from Korea, 35 from Taiwan, 32 from China, 20 from Hong Kong, 15 from Australia, 6 from Egypt, 3 from Bangladesh, and 1 from South Africa) were tested by both the **assay** of Okamoto et al. (H. Okamoto, Y. Sugiyama, S. Okada, K. Kurai, Y. Akahane, Y. Sugai, T. Tanaka, K. Sato, F. Tsuda, Y. Miyamura, and M. Mayumi, J. Gen. Virol. 73:673-679, 1992) and this new genotyping system. Comparison of the results showed concordant results for 539 samples (88.8%). Of the 68 samples with discordant results, the nucleotide sequences of the HCV isolates were determined in 23, and their **genotypes** were determined by molecular evolutionary analysis. In all 23 samples, the assignment of **genotype** by our new genotyping system was correct. This genotyping system may be useful for large-scale determination of HCV **genotypes** in clinical studies.

21/3,AB/33 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09193923 96432287 PMID: 8835353
Influence of viraemia and genotype **upon serological reactivity in screening assays for antibody to** hepatitis C virus.
Dhaliwal SK; Prescott LE; Dow BC; Davidson F; Brown H; Yap PL; Follett EA ; Simmonds P
Department of Medical Microbiology, University of Edinburgh, United Kingdom.
Journal of medical virology (UNITED STATES) Feb 1996, 48 (2) p184-90 , ISSN 0146-6615 Journal Code: I9N
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Detection of antibody to recombinant proteins derived from **hepatitis C virus** (HCV) **genotype** 1 represents the principal method for diagnosis of HCV infection. A method was developed for quantifying antibody reactivity in two third-generation enzyme immunoassays (Ortho **EIA** 3.0 and

Murex VK48), and the influence of viraemia, HCV **genotype** , and host factors such as age, gender, and risk group upon antibody levels were investigated in a consecutive series of 117 anti-HCV-positive volunteer blood donors. Viraemic donors (as assessed by the polymerase chain reaction; PCR) showed significantly higher levels of anti-HCV by the Ortho **EIA** than those who were nonviraemic (adjusted mean difference of 10.1 fold after multiple regression analysis). The only other factor to influence significantly antibody level was **genotype** , where it was found that donors infected with type 1 showed 4 to 4.5 times greater serological reactivity by the Ortho **assay** than those infected with type 2 or 3. Antibody levels by the Ortho **assay** correlated closely to those detected by the Murex VK48 **assay** , and similar differences between PCR-positive and negative donors and between those infected with different **genotypes** were found. Differences in serological reactivity between **genotypes** indicate that a large proportion of epitopes of the type 1a or 1b recombinant proteins used in current assays are **genotype** specific. Variation in sensitivity of screening assays for different **genotypes** is of potential concern when used in countries where non-type 1 **genotypes** predominate in the blood donor or patient population.

21/3,AB/37 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09130818 97103513 PMID: 8947884
Hepatitis C virus genotypes **in chronic hepatitis C of children.**
Bortolotti F; Vajro P; Balli F; Giacchino R; Crivellaro C; Barbera C; Pontisso P; Nebbia G; Zancan L; Bertolini A; Alberti A
Clinica Medica 2, Padua, Italy.
Journal of viral hepatitis (ENGLAND) Nov 1996, 3 (6) p323-7, ISSN 1352-0504 Journal Code: CG0
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Several **hepatitis C virus** (HCV) **genotypes** have been recently identified and **genotype** 1b has been correlated with severe liver disease and a poor response to interferon therapy. HCV infection in children is an interesting model for evaluation of the relationship between HCV **genotypes** and liver disease, because of its relatively short duration and the infrequent association with confounding cofactors. We have investigated HCV **genotypes** , using a dot-blot hybridization **assay** with **genotype** -specific probes, in 36 Italian children with chronic hepatitis C who were otherwise well and had no other underlying disease. Only four patients were symptomatic; liver histology, obtained in 33 patients, showed minimal hepatitis in 17 and mild chronic hepatitis in 16. Infection with HCV **genotype** 1b was found in 55.5% of patients, with a peak prevalence of 83% in children from southern Italy ($P < 0.05$ vs other regions). The remaining children were infected with HCV **genotype** 1a (16.6%), **genotype** 2 (11.1%), and mixed (10.9%) or undetermined (2.7%) **genotypes** . In one patient, HCV viraemia was never detected. There was no statistically significant correlation between **genotype** and age, sex, source of infection, alanine aminotransferase pattern and histological activity index. These results indicate that **genotype** 1 b is widespread among Italian children with chronic hepatitis C, although with significant geographical variations. It is not associated with a more severe liver disease, therefore suggesting that the greater severity of liver disease recently reported in adults could reflect the cumulative effects of disease duration and of interfering cofactors.

21/3,AB/47 (Item 47 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08973992 96269515 PMID: 8669088
Third-generation recombinant immunoblot assay : **comparison of reactivities according to** hepatitis C virus genotype.
Dow BC; Munro H; Buchanan I; Follett EA; Davidson F; Yap PL; Simmonds P
Scottish National Blood Transfusion Service Microbiology Reference Unit, Regional Virus Laboratory, Ruchill Hospital, Glasgow, United Kingdom.
Transfusion (UNITED STATES) Jun 1996, 36 (6) p547-51, ISSN 0041-1132 Journal Code: WDN
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Recombinant immunoblot **assay** (RIBA) is widely used as a supplemental test in **hepatitis C virus** (HCV) confirmatory algorithms. As this **assay** is based on HCV type 1, its performance was examined with the common European HCV **genotypes** (1, 2, and 3). STUDY DESIGN AND METHODS: A study was performed to retest in third-generation RIBA (RIBA-3) all 146 second-generation RIBA (RIBA-2)-positive polymerase chain reaction-positive samples detected by second-generation enzyme-linked immunosorbent assays and having known HCV **genotypes** (74 HCV type 1, 21 type 2, 51 type 3). RIBA band intensities were examined according to HCV **genotype** . An additional 90 RIBA-3-confirmed PCR-positive samples (47 HCV type 1, 5 type 2, 38 type 3) detected by third-generation enzyme-linked immunosorbent assays were also examined. RESULTS: In the first group of 146 samples, the RIBA-3 NS4 (c100p) band showed a marked improvement in sensitivity for the detection of HCV types 2 and 3 over that of the c100 antigen of RIBA-2, but the mean band intensities of HCV types 2 and 3 remained significantly lower than those of type 1. Improved sensitivity of the NS3 band of RIBA-3 to HCV type 3 was also apparent, but, again, the mean band intensity measured was lower for type 3 than for either type 1 or type 2. The c22 band of RIBA-2 and RIBA-3 exhibited equal sensitivity for all HCV **genotypes** . These differences were also apparent when RIBA-3 was used in conjunction with third-generation enzyme-linked immunosorbent assays. CONCLUSION: The current RIBA-3 lacks sensitivity to the NS4 antibody for HCV types 2 and 3. The incorporation of type-specific components to other **genotypes** for NS4 (and NS3) antigens should be considered by the manufacturers.

21/3,AB/50 (Item 50 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08869369 96196136 PMID: 8627040
Levels of hepatitis C virus **in blood donors infected with different viral** genotypes. **International HCV Collaborative Study Group.**
Smith DB; Davidson F; Yap P; Brown H; Kolberg J; Detmer J; Urdea M; Simmonds P; International HCV Collaborati
Department of Medical Microbiology, University of Edinburgh, United Kingdom.
Journal of infectious diseases (UNITED STATES) Mar 1996, 173 (3) p727-30, ISSN 0022-1899 Journal Code: IH3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The level of **hepatitis C virus** (HCV) in the serum of 337 blood donors infected with different viral **genotypes** was investigated by branched DNA **assay** . Viral **genotype** was deduced by restriction analysis of the virus 5'-noncoding region. Samples included **genotypes** 1a, 1b, 2a, 2b, 3,4,5, and 6. Multivariate analysis revealed that the ranges of HCV levels were similar for all viral **genotypes** and subtypes (P=.18), with the possible exception of **genotype** 4. Virus levels were significantly lower in female than in male subjects (P<.001) but did not correlate with donor age (P=.06) or **genotype** or with donor age, sex, or country. These results indicate a similar replicative capacity in vivo for different HCV

genotypes and clarify the influence of host and virus factors on disease severity and responsiveness to interferon treatment.

21/3,AB/57 (Item 57 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08790249 97201593 PMID: 9049379
Use of NS-4 peptides to identify type-specific antibody to hepatitis C virus genotypes **1, 2, 3, 4, 5 and 6.**
Bhattacherjee V; Prescott LE; Pike I; Rodgers B; Bell H; El-Zayadi AR; Kew MC; Conradie J; Lin CK; Marsden H; et al
Edinburgh and South East Scotland Blood Transfusion Service, Royal Infirmary of Edinburgh, UK.
Journal of general virology (ENGLAND) Jul 1995, 76 (Pt 7) p1737-48, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The 5' end of the NS-4 protein of different **genotypes** of **hepatitis C virus** (HCV) is highly variable in nucleotide and inferred amino acid sequence, with frequent predicted amino acid substitutions between all six of the major HCV **genotypes** described to date. This region has been shown to be antigenic by epitope mapping, and elicits antibody in HCV-infected individuals with a detectable type-specific component. We have used this sequence data to specify branched peptides for an indirect binding/competition **assay** to detect type-specific antibody to each major **genotype** . A total of 183 out of 210 samples (87%) from blood donors and patients with chronic hepatitis C infected with **genotypes** 1 to 6 showed detectable type-specific antibody to NS-4 peptides that in almost all cases (> 97 %) corresponded to the **genotype** detected by a PCR typing method. These findings demonstrate the existence of major antigenic differences between **genotypes** of HCV, and indicate how infection with different variants of HCV may be detected by a serological test.

21/3,AB/60 (Item 60 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08767876 95248766 PMID: 7537347
Genotype **-dependent serologic reactivities in patients infected with** hepatitis C virus **in the United States.**
Zein NN; Rakela J; Persing DH
Division of Gastroenterology and Internal Medicine, Mayo Clinic Rochester, Minnesota 55905, USA.
Mayo Clinic proceedings (UNITED STATES) May 1995, 70 (5) p449-52, ISSN 0025-6196 Journal Code: LLY
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
OBJECTIVE: To evaluate the serologic reactivities in patients infected with different **hepatitis C virus** (HCV) **genotypes** to four HCV proteins that are components of the second-generation recombinant immunoblot **assay** . MATERIAL AND METHODS: Serum samples from 36 patients with chronic HCV infection were obtained. RNA was extracted by using chaotropic lysis and isopropanol precipitation. Reverse-transcriptase polymerase chain reaction of the NS-5 region was performed, followed by automated single-pass dideoxy sequencing of desalted amplification products. Classification of isolated HCV subtypes was based on Simmonds' system. All samples were tested for antibodies to proteins 5-1-1, C100-3, C33c, and C22-3 with the second-generation recombinant immunoblot **assay** . RESULTS: Reactivity to protein 5-1-1 was significantly lower for patients with **genotypes** 2b and 3a than for those infected with HCV types 1a or 1b

(P < 0.05). Antibody reactivity to the C100-3 protein was also reduced in patients infected with HCV types 2b and 3a. CONCLUSION: These data indicate that the **genotype** -dependent differences in serologic reactivities are substantial among patients with chronic HCV infection.

21/3,AB/77 (Item 77 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08412258 94299818 PMID: 7913097
Geographical distribution of hepatitis C virus genotypes **in blood donors: an international collaborative survey.**
McOmish F; Yap PL; Dow BC; Follett EA; Seed C; Keller AJ; Cobain TJ; Krusius T; Kolho E; Naukkarinen R; et al
Edinburgh and South East Scotland Blood Transfusion Service, Royal Infirmary of Edinburgh, United Kingdom.
Journal of clinical microbiology (UNITED STATES) Apr 1994, 32 (4) p884-92, ISSN 0095-1137 Journal Code: HSH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The frequency of infection with the six classified major **genotypes** of **hepatitis C virus** (HCV) was investigated in 447 infected volunteer blood donors from the following nine countries: Scotland, Finland, The Netherlands, Hungary, Australia, Egypt, Japan, Hong Kong, and Taiwan. Viral sequences in plasma from blood donors infected with HCV were amplified in the 5'-noncoding region and were typed by restriction fragment length polymorphism analysis. Electrophoresis of DNA fragments produced by cleavage with HaeIII-RsaI and ScrFI-HinfI allowed HCV types 1 (or 5), 2, 3, 4, and 6 to be identified. Further analysis with MvaI-HinfI allowed sequences of the type 5 **genotype** to be distinguished from sequences of the type 1 **genotype** . Types 1, 2, and 3 accounted for almost all infections in donors from Scotland, Finland, The Netherlands, and Australia. Types 2 and 3 were not found in the eastern European country (Hungary), where all but one of the donors were infected with type 1. Donors from Japan and Taiwan were infected only with type 1 or 2, while types 1, 2, and 6 were found in those from Hong Kong. HCV infection among Egyptians was almost always by type 4. Donors infected with HCV type 1 showed broad serological reactivity with all four antigens of the second generation Chiron RIBA-2 **assay** (Chiron Corporation, Emeryville, Calif.), while infection with divergent HCV **genotypes** elicited antibodies mainly reactive to c22-3 and c33c. Reactivities with antibodies 5-1-1 and c100-3 were infrequent and were generally weak, irrespective of the geographical origin of the donor.(ABSTRACT TRUNCATED AT 250 WORDS)

21/3,AB/78 (Item 78 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08411624 94292119 PMID: 7517384
Diagnostic and clinical implications of the different genotypes **of** hepatitis C virus.
Bukh J; Miller RH
Hepatitis Viruses Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
Hepatology (UNITED STATES) Jul 1994, 20 (1 Pt 1) p256-9, ISSN 0270-9139 Journal Code: GBZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

21/3,AB/81 (Item 81 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07144260 93388890 PMID: 7690782
Genotype **dependence of** hepatitis C virus **antibodies detectable by the first-generation enzyme-linked immunosorbent** assay **with C100-3 protein.**
Nagayama R; Tsuda F; Okamoto H; Wang Y; Mitsui T; Tanaka T; Miyakawa Y; Mayumi M
First Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan.
Journal of clinical investigation (UNITED STATES) Sep 1993, 92 (3) p1529-33, ISSN 0021-9738 Journal Code: HS7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Hepatitis C virus (HCV) samples in 155 sera, from patients with chronic non-A, non-B liver disease and blood donors, were grouped into four **genotypes** (I, II, III, and IV) by amplification of core-gene sequences by polymerase chain reaction with type-specific primers. HCV **genotypes** were compared with various HCV-associated antibodies detectable by the first-generation **ELISA** (**ELISA** -1) with C100-3 protein and a second-generation immunoblot **assay** with four recombinant HCV proteins. Antibodies to C100-3 protein and those to its subsequence (5-1-1) were detected in 13 (93%) and 12 (86%), respectively, of 14 sera with **genotype** I HCV; 56 (79%) and 58 (82%) of 71 sera with **genotype** II; 13 (34%) and 6 (16%) of 38 sera with **genotype** III; and 11 (34%) and 4 (13%) of 32 sera with **genotype** IV. Amino acid sequences of C100-3 of **genotype** I HCV are conserved by approximately 90% in **genotype** II, but only by approximately 75% in **genotypes** III and IV. The sensitivity of **ELISA** -1, therefore, would be influenced by heterogeneity in C100-3 sequences of different **genotypes** .

21/3,AB/84 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10745577 BIOSIS NO.: 199799366722
New hepatitis C virus **(HCV) genotyping system that allows for identification of HCV** genotypes **1a, 1b, 2a, 2b, 3a, 3b, 4, 5a, and 6a.**
AUTHOR: Ohno Tomoyoshi(a); Mizokami Masashi; Wu Rong-Rong; Saleh Mohamed G; Ohba Ken-Ichi; Orito Etsuro; Mukaide Motokazu; Williams Roger; Lau Johnson Y M
AUTHOR ADDRESS: (a)Sect. Hepatobiliary Dis., Div. Gastroenterol. Hepatol. Nutr., Dep. Med., Univ. Florida, Gainesvi**USA
JOURNAL: Journal of Clinical Microbiology 35 (1):p201-207 1997
ISSN: 0095-1137
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recent studies have focused on whether different **hepatitis C virus** (HCV) **genotypes** are associated with different profiles of pathogenicity, infectivity, and response to antiviral therapy. The establishment of a simple and precise genotyping system for HCV is essential to address these issues. A new genotyping system based on PCR of the core region with **genotype** -specific PCR primers for the determination of HCV **genotypes** 1a, 1b, 2a, 2b, 3a, 3b, 4, 5a, and 6a was developed. A total of 607 samples (379 from Japan, 63 from the United States, 53 from Korea, 35 from Taiwan, 32 from China, 20 from Hong Kong, 15 from Australia, 6 from Egypt, 3 from Bangladesh, and 1 from South Africa) were tested by both the **assay** of Okamoto et al. (H. Okamoto, Y. Sugiyama, S. Okada, K. Kurai, Y. Akahane, Y. Sugai, T. Tanaka, K. Sato, F. Tsuda, Y. Miyamura, and M. Mayumi, J. Gen. Virol. 73:673-679, 1992)

and this new genotyping system. Comparison of the results showed concordant results for 539 samples (88.8%). Of the 68 samples with discordant results, the nucleotide sequences of the HCV isolates were determined in 23, and their **genotypes** were determined by molecular evolutionary analysis. In all 23 samples, the assignment of **genotype** by our new genotyping system was correct. This genotyping system may be useful for large-scale determination of HCV **genotypes** in clinical studies.

1997

21/3,AB/88 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10572901 BIOSIS NO.: 199699194046
Genotypes of hepatitis C virus **isolates from different parts of the world.**
AUTHOR: Guertler L G(a); Roggendorf M; Driesel G; Hoehne M; Viazov S
AUTHOR ADDRESS: (a)Max von Pettenkofer Inst. Hygiene und Medizinische Mikrobiol., Univ. Muenchen, Pettenkofer Str. **Germany
JOURNAL: Archives of Virology Supplement 0 (11):p195-202 1996
ISSN: 0939-1983
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English
1996

21/3,AB/94 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10082953 BIOSIS NO.: 199598537871
A second generation line probe assay **(LiPA) for the detection of the 6 most common** hepatitis C virus genotypes.
AUTHOR: Stuyver L; Wyseur A; Verpooten G; Maertens G
AUTHOR ADDRESS: Innogenetics, Ghent**Belgium
JOURNAL: Hepatology 22 (4 PART 2):p496A 1995
CONFERENCE/MEETING: 46th Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Diseases Chicago, Illinois, USA November 3-7, 1995
ISSN: 0270-9139
RECORD TYPE: Citation
LANGUAGE: English
1995

21/3,AB/96 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09636866 BIOSIS NO.: 199598091784
Serological Reactivity and Viral Genotypes **in** Hepatitis C Virus **Infection.**
AUTHOR: Maggi F; Vatteroni M L; Pistello M; Avio C M; Cecconi N; Panicucci F; Bendinelli M(a)
AUTHOR ADDRESS: (a)Dip. Biomed., Univ. Pisa, via San Zeno 35, I-56127 Pisa **Italy
JOURNAL: Journal of Clinical Microbiology 33 (1):p209-211 1995
ISSN: 0095-1137
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Patients infected with **hepatitis C virus** (HCV) were examined with four commercial HCV immunoblotting assays and for anti-GOR antibody to ascertain whether serological findings varied with the **genotype** of the infecting virus. The results indicate that patients infected with different HCV **genotypes** tend to show different immunoblotting profiles, mainly due to a low prevalence of antibodies to the viral region NS4 in patients infected with **genotypes** III and IV. Differences were more evident with second- than with third-generation assays. Patients infected with **genotype** IV exhibited a lower prevalence of anti-GOR antibody than patients infected with other **genotypes** .

1995
?

21/3,AB/102 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05891110 Genuine Article#: XE591 Number of References: 26
Title: Serological determination of hepatitis C virus genotype: **Comparison which a standardized genotyping** assay (ABSTRACT AVAILABLE)
Author(s): Pawlotsky JM (REPRINT) ; Prescott L; Simmonds P; Pellet C; LaurentPuig P; Labonne C; Darthuy F; Remire J; Duval J; Buffet C; Etienne JP; Dhumeaux D; Dussaix E
Corporate Source: UNIV PARIS 12,HOP HENRI MONDOR, DEPT BACTERIOL & VIROL, SERV BACTERIOL VIROL/F-94010 CRETEIL//FRANCE/ (REPRINT); UNIV PARIS 12,HOP HENRI MONDOR, DEPT GASTROENTEROL & HEPATOL/F-94010 CRETEIL//FRANCE/; UNIV PARIS 11,HOP BICETRE, DEPT GASTROENTEROL & HEPATOL/LE KREMLIN BICETRE//FRANCE/; UNIV PARIS 11,HOP BICETRE, DEPT BACTERIOL & VIROL/LE KREMLIN BICETRE//FRANCE/; UNIV EDINBURGH,SCH MED, DEPT MED MICROBIOL/EDINBURGH EH8 9AG/MIDLOTHIAN/SCOTLAND/
Journal: JOURNAL OF CLINICAL MICROBIOLOGY, 1997, V35, N7 (JUL), P1734-1739
ISSN: 0095-1137 Publication date: 19970700
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
Language: English Document Type: ARTICLE
Abstract: In patients with chronic hepatitis C. determination of **hepatitis C virus** (HCV) **genotype** could be routinely run in the future to tailor treatment schedules. The suitabilities of two versions of a serological, so-called serotyping **assay** (Murex HCV Serotyping **Assay** version 1-3 [SA1-3] and Murex HCV Serotyping **Assay** version 1-6 [SA1-6]; Murex Diagnostics Ltd.), based on the detection of **genotype** -specific antibodies directed to epitopes encoded by the NS4 region of the genome, for the routine determination of HCV **genotypes** were studied. The results were compared with those of a molecular biology-based genotyping method (HCV Line Probe **Assay** [INNO-LiPA HCV]; Innogenetics S.A.), based on hybridization of PCR products onto **genotype** -specific probes designed in the 5' noncoding region of the genome, obtained with pretreatment serum samples from 88 patients with chronic hepatitis C eligible for interferon therapy, Definitive genotyping was performed by sequence analysis of three regions of the viral genome in all samples with discrepant typing results found among at least two of the three assays studied. In all instances, sequence analysis confirmed the result of the INNO-LiPA HCV test. The sensitivity of SA1-3 was 75% relative to the results obtained by the genotyping **assay** . The results were concordant with those of genotyping for 92% of the samples typeable by SA1-3, The sensitivity of SA1-6 was 89% relative to the results obtained by the genotyping **assay** , The results mere concordant with those of genotyping for 94% of the samples typeable by SA1-6. Overall SA1-6 had increased sensitivity relative to Sk1-3 but remained less sensitive than the gene typing **assay** on the basis of PCR amplification of HCV RNA. Cross-reactivities between different HCV **genotypes** could be responsible for the mistyping of 8 (SA1-3) and 6% (SA1-6) of the samples, Subtyping of 1a and 1b is still not possible with the existing peptides, but discriminating between subtypes may not be necessary for routine use.

21/3,AB/107 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05337020 Genuine Article#: VQ934 Number of References: 37
Title: THE GOLD-STANDARD, ACCURACY, AND THE CURRENT CONCEPTS - HEPATITIS-C VIRUS GENOTYPE **AND VIREMIA**
Author(s): OHNO T; LAU JYN

Corporate Source: UNIV FLORIDA,DEPT MED,SECT HEPATOBILIARY DIS,DIV GASTROENTEROL & HEPATOL & NUTR,POB 100214/GAINESVILLE//FL/32611; UNIV FLORIDA,DEPT MED,SECT HEPATOBILIARY DIS,DIV GASTROENTEROL & HEPATOL & NUTR/GAINESVILLE//FL/32611
Journal: HEPATOLOGY, 1996, V24, N5 (NOV), P1312-1315
ISSN: 0270-9139
Language: ENGLISH Document Type: EDITORIAL MATERIAL

21/3,AB/119 (Item 20 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04139041 Genuine Article#: RH280 Number of References: 46
Title: USE OF NS-4 PEPTIDES TO IDENTIFY TYPE-SPECIFIC ANTIBODY TO HEPATITIS- C VIRUS GENOTYPE-**1,** GENOTYPE-**2,** GENOTYPE-**3,** GENOTYPE-**4,** GENOTYPE-**5 AND** GENOTYPE-**6** (Abstract Available)
Author(s): BHATTACHERJEE V; PRESCOTT LE; PIKE I; RODGERS B; BELL H; ELZAYADI AR; KEW MC; CONRADIE J; LIN CK; MARSDEN H; SAEED AA; PARKER D; YAP PL; SIMMONDS P
Corporate Source: UNIV EDINBURGH,DEPT MED MICROBIOL,TEVIOT PL/EDINBURGH EH8 9AG/MIDLOTHIAN/SCOTLAND/; UNIV EDINBURGH,DEPT MED MICROBIOL/EDINBURGH EH89AG/MIDLOTHIAN/SCOTLAND/; ROYAL EDINBURGH & ASSOCIATED HOSP,EDINBURGH & SE SCOTLAND BLOOD TRANSFUS SERV/EDINBURGH EH3 9HB/MIDLOTHIAN/SCOTLAND/; MUREX DIAGNOST LTD/DARTFORD DA1 5LR/KENT/ENGLAND/; AKER UNIV HOSP,HEPATOL UNIT/N-0514 OSLO 5//NORWAY/; CAIRO LIVER CTR/CAIRO//EGYPT/; UNIV WITWATERSRAND/JOHANNESBURG 2193//SOUTH AFRICA/; NATAL INST IMMUNOL/DURBAN//SOUTH AFRICA/; HONG KONG RED CROSS/KOWLOON//HONG KONG/; INST VIROL/GLASGOW G11 5JR/LANARK/SCOTLAND/; RIYADH ARMED FORCES HOSP/RIYADH 11159//SAUDI ARABIA/
Journal: JOURNAL OF GENERAL VIROLOGY, 1995, V76, JUL (JUL), P1737-1748
ISSN: 0022-1317
Language: ENGLISH Document Type: ARTICLE
Abstract: The 5' end of the NS-4 protein of different **genotypes** of **hepatitis C virus** (HCV) is highly variable in nucleotide and inferred amino acid sequence, with frequent predicted amino acid substitutions between all six of the major HCV **genotypes** described to date. This region has been shown to be antigenic by epitope mapping, and elicits antibody in HCV-infected individuals with a detectable type-specific component. We have used this sequence data to specify branched peptides for an indirect binding/competition **assay** to detect type-specific antibody to each major **genotype** . A total of 183 out of 210 samples (87%) from blood donors and patients with chronic hepatitis C infected with **genotypes** 1 to 6 showed detectable type-specific antibody to NS-4 peptides that in almost all cases (> 97%) corresponded to the **genotype** detected by a PCR typing method. These findings demonstrate the existence of major antigenic differences between **genotypes** of HCV, and indicate how infection with different variants of HCV may be detected by a serological test.

21/3,AB/123 (Item 24 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03387231 Genuine Article#: PC242 Number of References: 26
Title: SEQUENCE-ANALYSIS OF THE CORE GENE OF 14 HEPATITIS- C VIRUS GENOTYPES (Abstract Available)
Author(s): BUKH J; PURCELL RH; MILLER RH
Corporate Source: NIAID,INFECT DIS LAB,HEPATITIS VIRUSES SECT/BETHESDA//MD/20892
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED

STATES OF AMERICA, 1994, V91, N17 (AUG 16), P8239-8243
ISSN: 0027-8424
Language: ENGLISH Document Type: ARTICLE
Abstract: We previously sequenced the 5' noncoding region of 44 isolates of **hepatitis C virus** (HCV), as well as the envelope 1 (E1) gene of 51 HCV isolates, and provided evidence for the existence of at least 6 major genetic groups consisting of at least 12 minor **genotypes** of HCV (i.e., **genotypes** I/1a, II/1b, III/2a, IV/2b, 2c, V/3a, 4a-4d, 5a, and 6a), We now report the complete nucleotide sequence of the putative core (C) gene of 52 HCV isolates that represent all or these 12 **genotypes** as well as two additional **genotypes** provisionally designated 4e and 4f that we identified in this study. The phylogenetic analysis of the C gene sequences was in agreement with that of the E1 gene sequences. A major division in the genetic distance was observed between HCV isolates of **genotype** 2 and those of the other **genotypes** in analysis of both the E1 and C genes. The C gene sequences of 9 **genotypes** have not been reported previously (i.e., **genotypes** 2c, 4a-4f, 5a, and 6a). Our analysis indicates that the C gene-based methods currently used to determine the HCV **genotype** , such as PCR with **genotype** -specific primers, should be revised in light of these data, We found that the predicted C gene was exactly 573 nt long in all 52 HCV isolates, with an N-terminal start codon and no in-frame stop codons. The nucleotide and predicted amino acid identities of the C gene sequences were in the range of 79.4-99.0% and 85.3-100%, respectively. Furthermore, we mapped universally conserved, as well as **genotype** -specific, nucleotide and deduced amino acid sequences of the C gene. The predicted C proteins of the different HCV **genotypes** shared the following features: (i) high content of proline residues, (ii) high content of arginine and lysine residues located primarily in three domains with 10 such residues invariant at positions 39-62, (iii) a cluster of 5 conserved tryptophan residues, (iv) two nuclear localization signals and a DNA-binding motif, (v) a potential phosphorylation site with a serine-proline motif, and (vi) three conserved hydrophilic domains that have been shown by others to contain immunogenic epitopes. Thus, we have extended analysis of the predicted C protein of HCV to all of the recognized **genotypes** , confirmed the existence of highly conserved regions of this important structural protein, and demonstrated that the genetic relatedness of HCV isolates is equivalent when analyzing the most conserved (i.e., C) and the most variable (i.e., E1) genes of the HCV genome.

21/3,AB/126 (Item 2 from file: 65)

02460391 INSIDE CONFERENCE ITEM ID: CN025695314
Serological assay **to determine** hepatitis C virus genotype: **comparison with PCR-based** hepatitis C virus **genotyping** assay **in patients with chronic hepatitis C treated with alpha interferon**
Martinot-Peignoux, M.; Pawlotsky, J. M.; Aumont, P.; Erlinger, S.
CONFERENCE: Hepatitis C virus: Genetic heterogeneity and viral load- International workshop; 2nd
HEPATITIS C VIRUS, 1997; NO 2 P: 101-106
John Libbey Eurotext, 1997
ISBN: 2742001417
LANGUAGE: English DOCUMENT TYPE: Conference Papers
CONFERENCE SPONSOR: Groupe Francais d'etudes moleculaires des hepatites
CONFERENCE LOCATION: Paris
CONFERENCE DATE: Mar 1996 (199603) (199603)

21/3,AB/144 (Item 3 from file: 94)

DIALOG(R)File 94:JICST-EPlus

02036434 JICST ACCESSION NUMBER: 94A0193578 FILE SEGMENT: JICST-E
Various related antibody in genotype **of** hepatitis C virus.
Serological characteristic of NS antibody.
SHIGETA KATSUYOSHI (1); IGUCHI AKIKO (1); KATO TADASHI (1); KUBOTA MANABU (1); SUGIMOTO MOTONOBU (1)
(1) Toho Univ., School of Medicine, Omori Hospital
Kanzo(Acta Hepatologica Japonica), 1994, VOL.35,NO.1, PAGE.93, TBL.1, REF.4
JOURNAL NUMBER: Z0006BAM ISSN NO: 0451-4203
UNIVERSAL DECIMAL CLASSIFICATION: 578.72/.76 616.3-071
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Short Communication
MEDIA TYPE: Printed Publication

21/3,AB/147 (Item 6 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01726656 JICST ACCESSION NUMBER: 93A0124409 FILE SEGMENT: JICST-E
Determination of hepatitis C virus genotype **and its clinical significance.**
OKAMOTO HIROAKI (1)
(1) Jichi Medical School
Kan, Tan, Sui, 1992, VOL.25,NO.5, PAGE.955-964, FIG.3, TBL.6, REF.9
JOURNAL NUMBER: Z0248BAQ ISSN NO: 0389-4991
UNIVERSAL DECIMAL CLASSIFICATION: 616.3-07
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication

21/3,AB/159 (Item 1 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00418230
NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES **AND THEIR USE AS PROPHYLACTIC, THERAPEUTIC AND DIAGNOSTIC AGENTS**
NOUVELLES SEQUENCES DE GENOTYPES **DU VIRUS DE L'HEPATITE C ET LEUR UTILISATION EN TANT QU'AGENTS PROPHYLACTIQUES, THERAPEUTIQUES ET DIAGNOSTIQUES**
Patent Applicant/Assignee:
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MAERTENS Geert
STUYVER Lieven
Patent and Priority Information (Country, Number, Date):
Patent: WO 9613590 A2-A3 19960509
Application: WO 95EP4155 19951023 (PCT/WO EP9504155)
Priority Application: EP 94870166 19941021; EP 95870076 19950628
Designated States: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TT UA UG US UZ VN KE LS MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 25103

English Abstract
The present invention relates to new genomic nucleotide sequences and amino acid sequences corresponding to the coding region of these genomes. The invention relates to new HCV types and subtypes sequences which are different from the known HCV types and subtypes sequences. More particularly, the present invention relates to new HCV type 7 sequences, new HCV type 9 sequences, new HCV type 10 and new HCV type 11 sequences. Also, the present invention relates to new HCV type 1 sequences of subtypes 1d, 1e, 1f and 1g; new HCV type 2 sequences of subtypes 2e, 2f, 2g, 2h, 2i, 2k and 2l; new HCV type 3 sequences of subtype 3g, new HCV type 4 sequences of subtypes 4k, 4l and 4m; a process for preparing them, and their use for diagnosis, prophylaxis and therapy. More particularly, the present invention provides new type- specific sequences of the Core, the E1 and the NS5 regions of new HCV types 7, 9, 10 and 11, as well as of new variants (subtypes) of HCV types 1, 2, 3 and 4. These new HCV sequences are useful to diagnose the presence of HCV type 1, and/or type 2, and/or type 3, and/or type 4, and/or type 7, and/or type 9, and/or type 10, and/or type 11 **genotypes** or serotypes in a biological sample. Moreover, the availability of these new type-specific sequences can increase the overall sensitivity of HCV detection and should also prove to be useful for prophylactic and therapeutic purposes.

Japanese Abstract
L'invention concerne de nouvelles sequences genomiques de nucleotides et d'acides amines correspondant a la region codante de ces genomes. L'invention concerne egalement des sequences nouvelles de types et de sous-types du virus de l'hepatite C, lesquelles sont differentes des sequences connues de types et de sous-types de ce virus. L'invention concerne plus particulierement des sequences nouvelles de type 7, type 9, type 10 et type 11 de ce virus. L'invention concerne encore des sequences nouvelles des sous-types 1d, 1e, 1f et 1g du type 1 dudit virus VHC; des sequences nouvelles des sous-types 2e, 2f, 2g, 2h, 2i, 2k et 2l du type 2 dudit virus VHC; des sequences nouvelles du sous-type 3g du type 3 du VHC, des sequences nouvelles des sous-types 4k, 4l et 4m du type 4 du VHC; ainsi qu'un procede de preparation de ces sequences et l'utilisation de celles-ci a des fins diagnostiques, prophylactiques et therapeutiques. En outre, l'invention concerne des sequences nouvelles specifiques a des types, des regions du noyau, et les regions E1 et NS5 des types nouveaux 7, 9, 10 et 11 du VHC, ainsi que de nouveaux (sous- types) des types 1, 2, 3 et 4 du virus VHC. Ces nouvelles sequences du virus de l'hepatite C sont utiles pour diagnostiquer, dans un echantillon biologique, la presence de **genotypes** ou serotypes du type 1, et/ou du type 2, et/ou du type 3, et/ou du type 4, et/ou du type 7, et/ou du type 9, et/ou du type 10, et/ou du type 11 du VHC. En outre, grace a ces nouvelles sequences disponibles, specifiques a des types, on peut ameliorer le taux global de detection du virus de l'hepatite C, lesdites sequences pouvant egalement etre utiles a des fins prophylactiques et therapeutiques.

21/3,AB/160 (Item 2 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00365212
NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES **AND THEIR USE AS THERAPEUTIC AND DIAGNOSTIC AGENTS**
NOUVELLES SEQUENCES DE GENOTYPES **DU VIRUS DE L'HEPATITE C ET LEUR UTILISATION EN TANT QU'AGENTS THERAPEUTIQUES ET DIAGNOSTIQUES**
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Inventor(s):
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Patent and Priority Information (Country, Number, Date):
Patent: WO 9425601 A2-A3 19941110
Application: WO 94EP1323 19940427 (PCT/WO EP9401323)
Priority Application: EP 93401099 19930427; EP 93402019 19930805
Designated States: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN AT BE CH DE FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 91246

English Abstract
The present invention relates to a polynucleic acid composition comprising or consisting of at least one polynucleic acid containing 8 or more contiguous nucleotides corresponding to a nucleotide sequence from the region spanning positions 417 to 957 of the Core/E1 region of HCV type 3; and/or the region spanning positions 4664 to 4730 of the NS3 region of HCV type 3; and/or the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type 3; and/or the region spanning positions 8 023 to 8 235 of the NS5 region of the BR36 subgroup of HCV type 3a; and/or the coding region of HCV type 4a starting at nucleotide 379 in the core region; and/or the coding region of HCV type 4; and/or the coding region of HCV type 5, with said nucleotide numbering being with respect to the numbering of HCV nucleic acids as shown in Table 1, and with said polynucleic acids containing at least one nucleotide difference with known HCV type 1, and/or HCV type 2 genomes in the above- indicated regions, or the complement thereof.

Japanese Abstract
L'invention concerne une composition d'acides polynucleiques comprenant au moins un acide polynucleique contenant 8 nucleotides contigus ou plus correspondant a une sequence nucleotidique provenant de la region couvrant les positions 417 a 957 de la region noyau/E1 du virus de l'hepatite C (VHC) de type 3; et/ou a la region couvrant les positions 4664 a 4730 de la region NS3 du VHC de type 3; et/ou a la region couvrant les positions 4892 a 5292 de la region NS3/4 du VHC de type 3; et/ou a la region couvrant les positions 8 023 a 8 235 de la region NS5 du sous-groupe BR36 du VHC de type 3a; et/ou a la region codante du VHC de type 4a commencant au niveau du nucleotide 379 dans la region noyau; et/ou a la region codante du VHC de type 4a commencant au niveau du nucleotide 379 dans la region noyau; et/ou a la region codante du VHC du type 4; et/ou a la region codante du VHC de type 5; la numerotation des nucleotides etant fonction de la numerotation des acides nucleiques du VHC conformement au tableau 1, lesdits acides polynucleiques contenant au moins une difference nucleotidique avec le VHC de type 1 connu, et/ou les genomes du VHC de type 2 dans les regions sus-mentionnees, ou leur complement.
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